

# Tracheal dimensions in human fetuses: an anatomical, digital and statistical study

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## Abstract

**Purpose** Rapid advances in perinatal medicine have resulted in increased number of various tracheo-bronchial interventions on fetal and neonatal airways. The present study was performed to compile normative data for external dimensions of the trachea at varying gestational age.

**Materials and methods** Using anatomical dissection, digital image analysis (NIS-Elements BR 3.0) and statistical analysis (ANOVA, regression analysis), a range of measurements (prebifurcation and bifurcation lengths, proximal and distal external transverse diameters, proximal external cross-sectional area, and external volume) for the trachea in 73 spontaneously aborted fetuses (39 male, 34 female) aged 14–25 weeks was examined.

**Results** No significant male–female differences were found ( $P > 0.05$ ). The prebifurcation and bifurcation lengths ranged from  $8.14 \pm 1.90$  to  $20.77 \pm 0.50$  mm and from  $2.23 \pm 0.25$  to  $5.77 \pm 0.76$  mm, according to the functions  $y = -54.291 + 23.940 \times \ln(\text{Age}) \pm 1.681$  ( $R^2 = 0.78$ ) and  $y = -10.756 + 4.860 \times \ln(\text{Age}) \pm 0.731$  ( $R^2 = 0.44$ ), respectively. Their relative growth, expressed as the bifurcation-to-prebifurcation length ratio, was stable from the age of 16 weeks and attained the value  $0.22 \pm 0.05$ . The proximal external transverse diameter of the trachea was greater (36 fetuses, 49.3%), smaller (34 fetuses, 46.6%) or

similar (3 fetuses, 4.1%), when compared to the distal external transverse diameter. The values for proximal and distal transverse diameters ranged from  $2.39 \pm 0.04$  to  $5.20 \pm 0.17$  mm and from  $2.42 \pm 0.20$  to  $4.93 \pm 0.08$  mm, expressed by the functions:  $y = -9.659 + 4.574 \times \ln(\text{Age}) \pm 0.313$  ( $R^2 = 0.79$ ) and  $y = -10.897 + 4.984 \times \ln(\text{Age}) \pm 0.327$  ( $R^2 = 0.81$ ). The values of proximal external cross-sectional area ranged from  $3.38 \pm 0.12$  to  $15.98 \pm 1.04$  mm<sup>2</sup>, according to the linear function  $y = -11.798 + 1.077 \times \text{Age} \pm 1.463$  ( $R^2 = 0.78$ ). The values of external volume of the trachea ranged from  $34.3 \pm 11.6$  to  $370.6 \pm 94.1$  mm<sup>3</sup> and generated the quadratic function  $y = -154.589 + 0.858 \times \text{Age}^2 \pm 34.196$  ( $R^2 = 0.87$ ).

**Conclusions** The tracheal parameters do not show male–female differences. The developmental dynamics of prebifurcation and bifurcation lengths and proximal and distal external transverse diameters of the trachea follow linear functions dependent on the natural logarithm of fetal age, its external cross-sectional area—according to a linear function, and its external volume—according to a quadratic function.

**Keywords** Trachea · Length · External transverse diameter · External cross-sectional area · External volume

## Introduction

Progress in perinatal medicine has led to the early diagnosis and treatment of respiratory diseases, and to the rapid development of fetal airway surgery [4, 9, 11, 15, 19].

The normative data for dimensions of the fetal trachea are still far from completed. To date, the growth of length and diameters has been reported as a proportional relationship, being expressed by a straight line [1, 2, 5, 16, 20].

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Few studies have assessed internal cross-sectional areas [3, 6, 13] and internal volumes [6, 13] of the trachea derived from chest CT scans in children and adults. However, no study has investigated external cross-sectional areas and external volumes of the trachea. Therefore, to improve the knowledge of tracheal quantitative morphology, our objectives were to investigate the following:

- age-specific reference intervals for prebifurcation and bifurcation lengths, proximal and distal external transverse diameters, proximal external cross-sectional area, and external volume of the trachea,
- the relative growth of bifurcation length in relation to prebifurcation length (bifurcation-to-prebifurcation length ratio),
- growth curves for normal development of the seven parameters studied,
- the influence of sex on the value of the parameters examined.

## Materials and methods

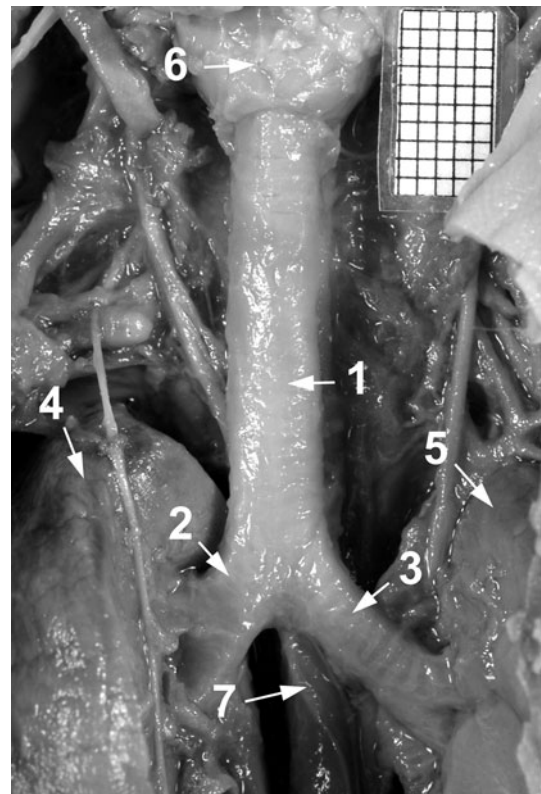
The study was carried out on 73 human fetuses of both sexes (39 male, 34 female) from spontaneous abortions or stillbirths, aged 14–25 weeks of gestation. Legal and ethical considerations were consistent with the rules of the University Research Ethics Committee (KB 189/2011). The fetal age was estimated on the basis of crown-rump length with reference to Iffy tables [10].

All specimens were immersed in 10% neutral formalin solution for 12–24 months for preservation. Dissection of the trachea and the main bronchi was performed according to the standard autopsy techniques, under tenfold magnification using a stereoscope with Huygens ocular. The fetuses were free of malformation affecting both laryngotracheal and cardiovascular structures, when assessed on macroscopic examination.

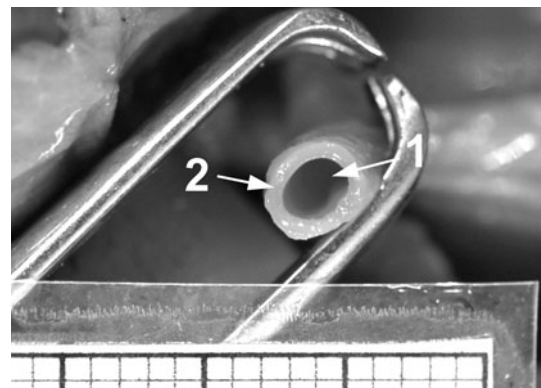
In each fetus, the trachea in situ with a millimeter scale was placed vertically to the optical lens axis, then recorded using Nikon D200 camera, and digitalized to TIFF images. Next, digital pictures of the trachea (Fig. 1) underwent quantitative analysis using digital image analysis (NIS-Elements BR 3.0, Nikon). At first length, proximal and distal external transverse diameters were measured, and after that cross sections (Fig. 2) were taken between the cricoid cartilage and the first tracheal cartilage rings.

For each subject the seven following measurements and calculations of the trachea were performed:

1. prebifurcation length, corresponding to the distance between the superior border of the first tracheal cartilage and the inferior border of the last tracheal cartilage,



**Fig. 1** The trachea and main bronchi in a male fetus aged 24 weeks: 1 trachea, 2 right main bronchus, 3 left main bronchus, 4 right lung, 5 left lung, 6 larynx, 7 esophagus



**Fig. 2** The trachea in cross section at the level of the first tracheal cartilage in a male fetus aged 18 weeks: 1 tracheal lumen, 2 tracheal wall

2. bifurcation length, corresponding to the distance between the inferior border of the last tracheal cartilage and the tracheal bifurcation,
3. bifurcation-to-prebifurcation length ratio,
4. proximal external transverse diameter, measured at the level of the first tracheal cartilage,
5. distal external transverse diameter, measured at the level of the last tracheal cartilage,
6. proximal external cross-sectional area, traced around the external border of the first tracheal cartilage,

**Table 1** Morphometric parameters of the fetal trachea

Fetal age (weeks)	Number of fetuses (n)	Prebifurcation length (mm)		Bifurcation length (mm)		External transverse diameter (mm)				External cross-sectional area (mm <sup>2</sup> )		External volume (mm <sup>3</sup> )	
		Mean	SD	Mean	SD	Proximal		Distal		Mean	SD	Mean	SD
						Mean	SD	Mean	SD				
14	2	8.14	1.90	2.23	0.25	2.39	0.04	2.42	0.20	3.38	0.12	34.3	11.6
15	1	9.66		2.58		3.00		2.23		5.32			
16	2	12.38	2.02	2.75	1.18	2.91	0.24	2.94	0.23	5.02	0.83	78.1	19.3
17	9	14.37	2.77	2.80	0.85	3.17	0.36	3.18	0.42	6.01	1.38		
18	10	14.96	0.89	3.51	0.76	3.57	0.33	3.55	0.43	7.59	1.40	146.0	40.9
19	7	17.26	0.92	3.68	0.81	3.95	0.33	3.84	0.20	9.29	1.54		
20	13	17.35	2.03	4.05	0.89	4.06	0.39	4.05	0.48	9.83	1.88	197.5	43.1
21	11	18.12	1.83	3.70	0.56	4.27	0.31	4.22	0.43	10.80	1.53		
22	5	20.42	1.91	3.97	0.80	4.53	0.21	4.54	0.18	12.17	1.15	296.1	58.2
23	6	20.63	3.00	4.55	1.48	4.92	0.73	4.82	0.38	14.57	4.32		
24	5	22.25	0.87	4.62	0.19	5.06	0.59	5.00	0.47	15.28	3.69	370.6	94.1
25	2	20.77	0.50	5.77	0.76	5.20	0.17	4.93	0.08	15.98	1.04		

**Table 2** An increase in values (per week) of morphometric parameters of the fetal trachea

Fetal age (weeks)	Prebifurcation length (mm per week)	Bifurcation length (mm per week)	External transverse diameter	
			Proximal (mm per week)	Distal (mm per week)
14	1.65	0.34	0.32	0.34
15	1.55	0.31	0.30	0.32
16	1.45	0.29	0.28	0.30
17	1.37	0.28	0.26	0.28
18	1.29	0.26	0.25	0.27
19	1.23	0.25	0.23	0.26
20	1.17	0.24	0.22	0.24
21	1.11	0.23	0.21	0.23
22	1.06	0.22	0.20	0.22
23	1.02	0.21	0.19	0.21
24	0.98	0.20	0.19	0.20

7. external volume, calculated by multiplying the sum of prebifurcation and bifurcation lengths by proximal external cross-sectional area.

All the parameters studied were plotted against fetal age so as to establish their growth. Finally, the results obtained were evaluated by the one-way ANOVA test for unpaired data and post hoc Bonferroni test. Regression analysis was used to derive the curve of best fit for each parameter versus gestational age. Coefficients of determination ( $R^2$ ) between each parameter and fetal age were estimated.

## Results

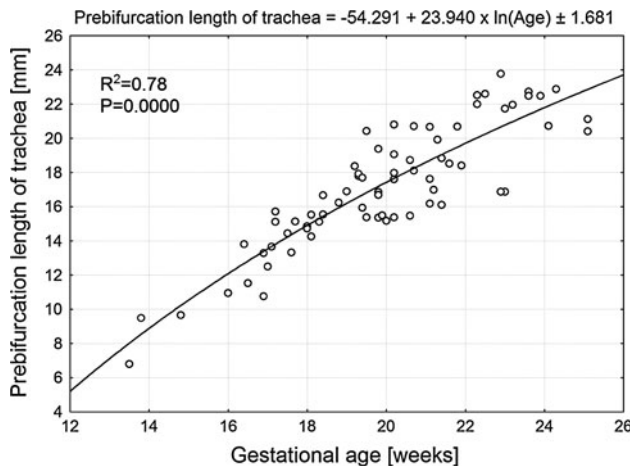
The results obtained are presented in Tables 1 and 2, and Figs. 3, 4, 5, 6, 7, 8, 9. The statistical analysis of examined

features of the trachea revealed no sex differences ( $P > 0.05$ ). Hence the morphometric values studied, regardless of sex, are included in Table 1. Conversely, the growth curves of best fit for the plot for each parameter studied against gestational age were statistically significant ( $P = 0.0000$ ).

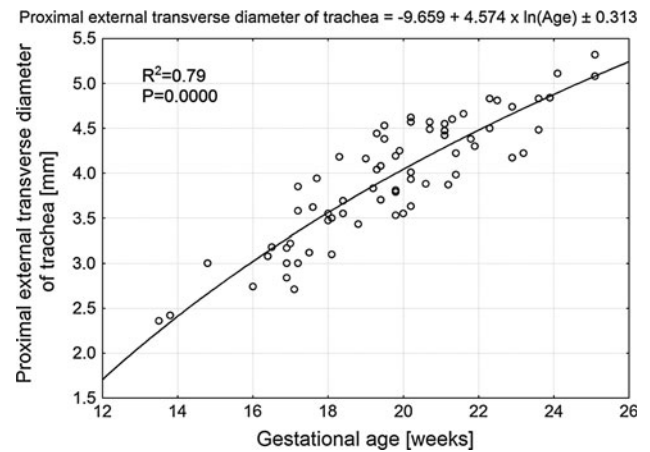
During the study period, the values of prebifurcation length ranged from  $8.14 \pm 1.90$  to  $20.77 \pm 0.50$  mm. The growth of prebifurcation length (Fig. 3) followed the linear function dependent on the natural logarithm of fetal age:  $y = -54.291 + 23.940 \times \ln(\text{Age}) \pm 1.681$  ( $R^2 = 0.78$ ).

The values of bifurcation length rose from  $2.23 \pm 0.25$  to  $5.77 \pm 0.76$  mm, according to the function:  $y = -10.756 + 4.860 \times \ln(\text{Age}) \pm 0.731$  ( $R^2 = 0.44$ ) (Fig. 4).

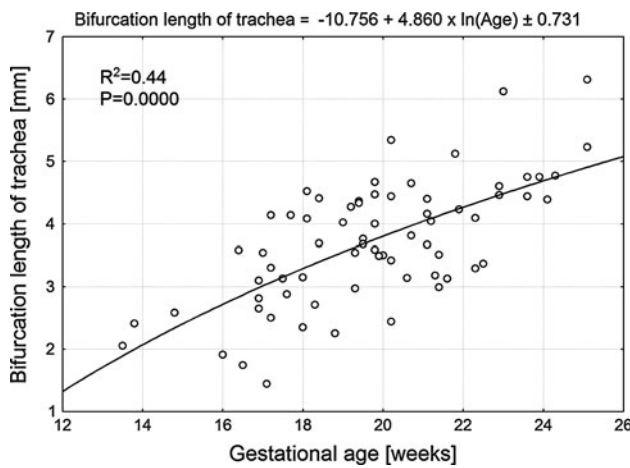
To take into account the relative tracheal growth, we calculated the bifurcation-to-prebifurcation length ratio.



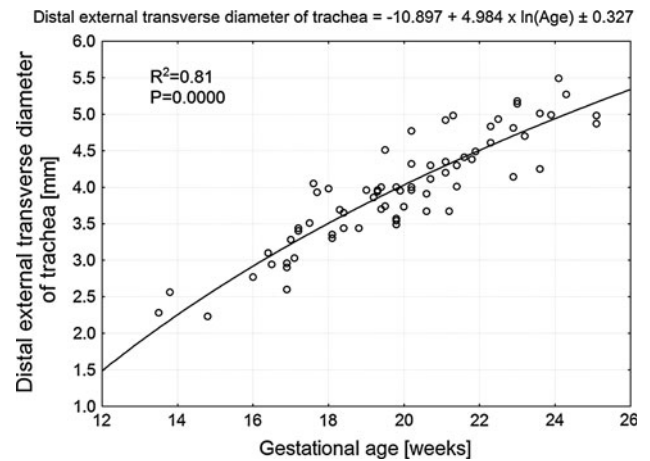
**Fig. 3** Regression line for prebifurcation length of the trachea versus gestational age



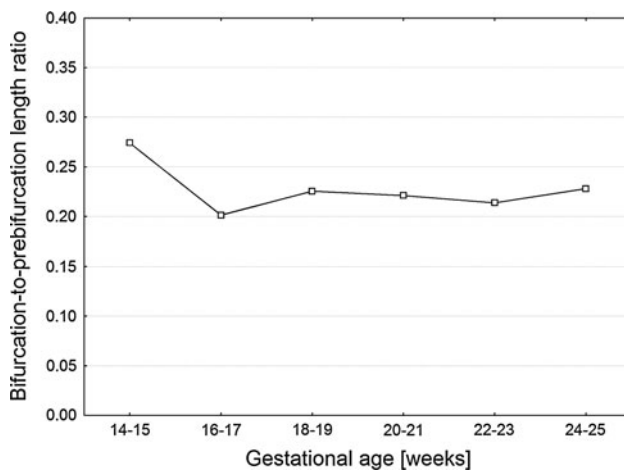
**Fig. 6** Regression line for proximal external transverse diameter of the trachea versus gestational age



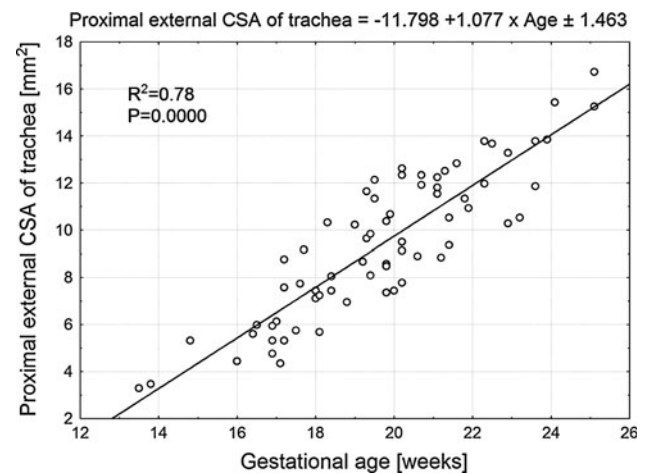
**Fig. 4** Regression line for bifurcation length of the trachea versus gestational age



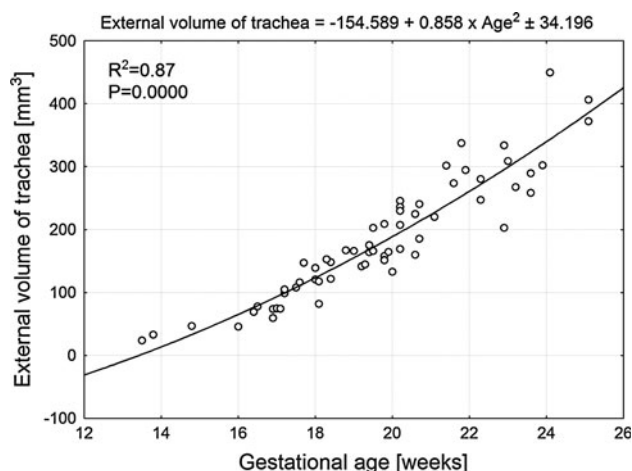
**Fig. 7** Regression line for distal external transverse diameter of the trachea versus gestational age



**Fig. 5** Bifurcation-to-prebifurcation length ratio of the trachea versus gestational age



**Fig. 8** Regression line for proximal external cross-sectional area of the trachea versus gestational age



**Fig. 9** Regression line for external volume of the trachea versus gestational age

Despite an increase in values of the two lengths studied, their relative growth expressed as the bifurcation-to-prebifurcation length ratio, plotted against gestational age, was stable from the age of 16 weeks and attained the value  $0.22 \pm 0.05$  (Fig. 5).

Proximal external transverse diameters of the trachea were greater (36 fetuses, 49.3%), smaller (34 fetuses, 46.6%) or the same (3 fetuses, 4.1%), when compared to distal external transverse diameters. The values for proximal transverse diameter ranged from  $2.39 \pm 0.04$  to  $5.20 \pm 0.17$  mm for the fetuses at 14 and 25 weeks of gestation, respectively. These results showed that proximal external transverse diameter as a function of fetal age (Fig. 6) was expressed by the regression  $y = -9.659 + 4.574 \times \ln(\text{Age}) \pm 0.313$  ( $R^2 = 0.79$ ). The increase in values of distal external transverse diameter ranged from  $2.42 \pm 0.20$  to  $4.93 \pm 0.08$  mm, and modeled the regression  $y = -10.897 + 4.984 \times \ln(\text{Age}) \pm 0.327$  ( $R^2 = 0.81$ ) (Fig. 7).

The growth dynamics of both the two tracheal lengths and external diameters were decreasing with advanced fetal age. When compared ages of 15 and 24 weeks, the growth (per week) in values was considerably smaller for each parameter, as follows: 1.65 versus 0.98 for prebifurcation length, 0.34 versus 0.20 for bifurcation length, 0.32 versus 0.19 and 0.34 versus 0.20 for proximal and distal external transverse diameters, respectively.

During the study period, the values of proximal external cross-sectional area for the trachea ranged from  $3.38 \pm 0.12$  to  $15.98 \pm 1.04$  mm<sup>2</sup>, according to the linear function  $y = -11.798 + 1.077 \times \text{Age} \pm 1.463$  ( $R^2 = 0.78$ ) (Fig. 8).

The values of its external volume ranged from  $34.3 \pm 11.6$  mm<sup>3</sup> in fetuses aged 14–15 weeks to  $370.6 \pm 94.1$  mm<sup>3</sup> in fetuses aged 24–25 weeks. The external volumetric growth of the trachea generated the quadratic function  $y = -154.589 + 0.858 \times \text{Age}^2 \pm 34.196$  ( $R^2 = 0.87$ ) (Fig. 9).

## Discussion

Reference data for tracheal length and external transverse diameters are scarce in human fetuses. In this anatomical study, digital image analysis (NIS-Elements BR 3.0) was used for measuring tracheal morphometric parameters in fetuses at the age of 14–25 weeks. No significant male–female differences for any of tracheal parameters were found in our sample, in keeping with the findings of some authors [1, 8, 14, 16] in relation to length and external diameters of the trachea. Conversely, significant sex differences in those tracheal measurements, being greater in males, were found in children [17], adolescents [7], and adults [12, 18].

A particular strength of this study results from the large number ( $n = 73$ ) of fetuses used to generate the growth curves. Of note, several transformations concerning tracheal length and diameters against fetal age were generated, but it was proven to be a non-linear correlation, being best described as a linear function dependent on the natural logarithm of age. Analysis of the variance revealed that these non-linear models were highly significant statistically (for each parameter  $P < 0.001$ ). However, most authors [1, 4, 5, 16] reported that both length and diameters of the trachea increased with advanced fetal age in a proportional fashion, being best described as a straight line. Fayoux et al. [5] presented linear relationships between tracheal length or diameter and fetal age, but without giving precise regression equations. Thus, based on Fig. 4 given by these authors, we calculated ourselves the following formula  $y = 0.909 \times \text{Age} + 0.61$  for tracheal length. Therefore, the present findings are not compatible with those autopsy studies, and provides novel data about the developmental dynamic of the parameters studied. This difference could be accounted for different methods of measurements used in those studies. Reference intervals for both prebifurcation and bifurcation lengths were constructed as follows: from  $8.14 \pm 1.90$  to  $20.77 \pm 0.50$  mm and from  $2.23 \pm 0.25$  to  $5.77 \pm 0.76$  mm. According to Harjeet et al. [8], the tracheal length (related to prebifurcation length) was  $12.72 \pm 2.50$  mm in fetuses with a crown-to-rump length (CRL) of 61–130 mm,  $17.48 \pm 2.89$  mm in fetuses with a CRL of 131–200 mm, and  $24.17 \pm 2.30$  mm in fetuses with a CRL of 201–270 mm. It is noteworthy, that the three groups of fetuses were related to ages of 13–18 weeks, 19–24 weeks, and 25–31 weeks, respectively. Therefore, the above mentioned results were smaller than those recorded in the present study.

In the material under examination, the tracheal growth was precisely expressed by the regressions:  $y = -54.291 + 23.940 \times \ln(\text{Age}) \pm 1.681$  for prebifurcation length and  $y = -10.756 + 4.860 \times \ln(\text{Age}) \pm 0.731$  for bifurcation length. Nevertheless as indicated in Fig. 5, both lengths



studied revealed a proportional evolution, since the bifurcation-to-prebifurcation length ratio did not change its value ( $0.22 \pm 0.05$ ) throughout the study period.

According to our results, the external transverse diameters of the trachea were found to increase from  $2.39 \pm 0.04$  to  $5.20 \pm 0.17$  mm and from  $2.42 \pm 0.20$  to  $4.93 \pm 0.08$  mm for proximal and distal ends of the trachea, respectively. Our numerical data are consistent with results obtained by Harjeet et al. [8]. In the three groups of fetuses aged 13–18, 19–24, and 25–31 weeks, the values of proximal transverse diameter were  $3.26 \pm 0.68$  mm,  $4.42 \pm 0.64$  mm, and  $5.35 \pm 0.42$  mm, respectively. We calculated the growth of proximal transverse diameter of the trachea in the material reported by Fayoux et al. [5], which followed the function  $y = 0.083 \times \text{Age} + 1.67$ . However, our measurements of tracheal diameters show their dependence on fetal age in accordance with the functions  $y = -9.659 + 4.574 \times \ln(\text{Age}) \pm 0.313$  for proximal external transverse diameter and  $y = -10.897 + 4.984 \times \ln(\text{Age}) \pm 0.327$  for the distal one. It should be emphasized that the growth in values for each parameter was smaller and smaller (Table 2) between ages of 14 and 25 weeks, that is in accordance with the course of a linear function dependent on the natural logarithm of age.

Among the tracheal parameters that we were able to measure, neither proximal external cross-sectional area nor external volume have so far been assessed in the literature. In the current study, we have shown that the proximal external cross-sectional area of the trachea varied between  $3.38 \pm 0.12$  and  $15.98 \pm 1.04$  mm<sup>2</sup>, in accordance with the function  $y = -11.798 + 1.077 \times \text{Age} \pm 1.463$ . Beyond doubt, the values of proximal external cross-sectional area of the trachea in the material under examination were much smaller than the values of its internal cross-sectional area ( $20\text{--}28$  mm<sup>2</sup>) recorded in neonates [3, 6].

As far as the external tracheal volume is concerned, it was found to increase from  $34.3 \pm 11.6$  mm<sup>3</sup> in fetuses aged 14–15 weeks to  $370.6 \pm 94.1$  mm<sup>3</sup> in fetuses aged 24–25 weeks, being related to the function  $y = -154.589 + 0.858 \times \text{Age}^2 \pm 34.196$ . The quadratic function turned out to be the best growth model for external volume of the trachea ( $R^2 = 0.87$ ). In our sample, the external volume of the trachea increased about 11-fold, which was related to the product of the tracheal length and its proximal external cross-sectional area that increased approximately 2.6-fold and 4.7-fold, respectively. Our recent studies, which are in progress, support the fact that the external volumetric growth is as many as about three times stronger than its internal volumetric growth. This fact is likely to be the consequence of an intensive evolution of tracheal wall thickness, which relatively reduces tracheal luminal volume.

The current autopsy study can be of interest to establish diagnostic criteria for tracheal malformations.

## Conclusions

1. The tracheal parameters do not show male–female differences.
2. The developmental dynamics of prebifurcation and bifurcation lengths, and proximal and distal external transverse diameters of the trachea follow linear functions dependent on the natural logarithm of fetal age, its proximal external cross-sectional area—according to a linear function and its external volume—according to a quadratic function.

**Conflict of interest** The authors declare that they have no conflict of interest.

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